Epidemiologia e clinica della patologia maligna della tiroide

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Surveillance, Epidemiology, and End Results Program

Cancer Stat Facts: Thyroid Cancer

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Statistics at a Glance

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At a Glance

Estimated New Cases in 2017	56,870
% of All New Cancer Cases	3.4%
Estimated Deaths in 2017	2,010
% of All Cancer Deaths	0.3%

Percent Surviving 5 Years

98.2%

2007–2013

Number of New Cases and Deaths per 100,000: The number of new cases of thyroid cancer was 14.2 per 100,000 men and women per year. The number of deaths was 0.5 per 100,000 men and women per year. These rates are age-adjusted and based on 2010–2014 cases and deaths.

Lifetime Risk of Developing Cancer: Approximately 1.2 percent of men and women will be diagnosed with thyroid cancer at some point during their lifetime, based on 2012–2014 data.

Prevalence of This Cancer: In 2014, there were an estimated 726,646 people living with thyroid cancer in the United States.

SEER Stat Fact Sheets, available at http://seer.cancer.gov/ statfacts/html/thyro.html

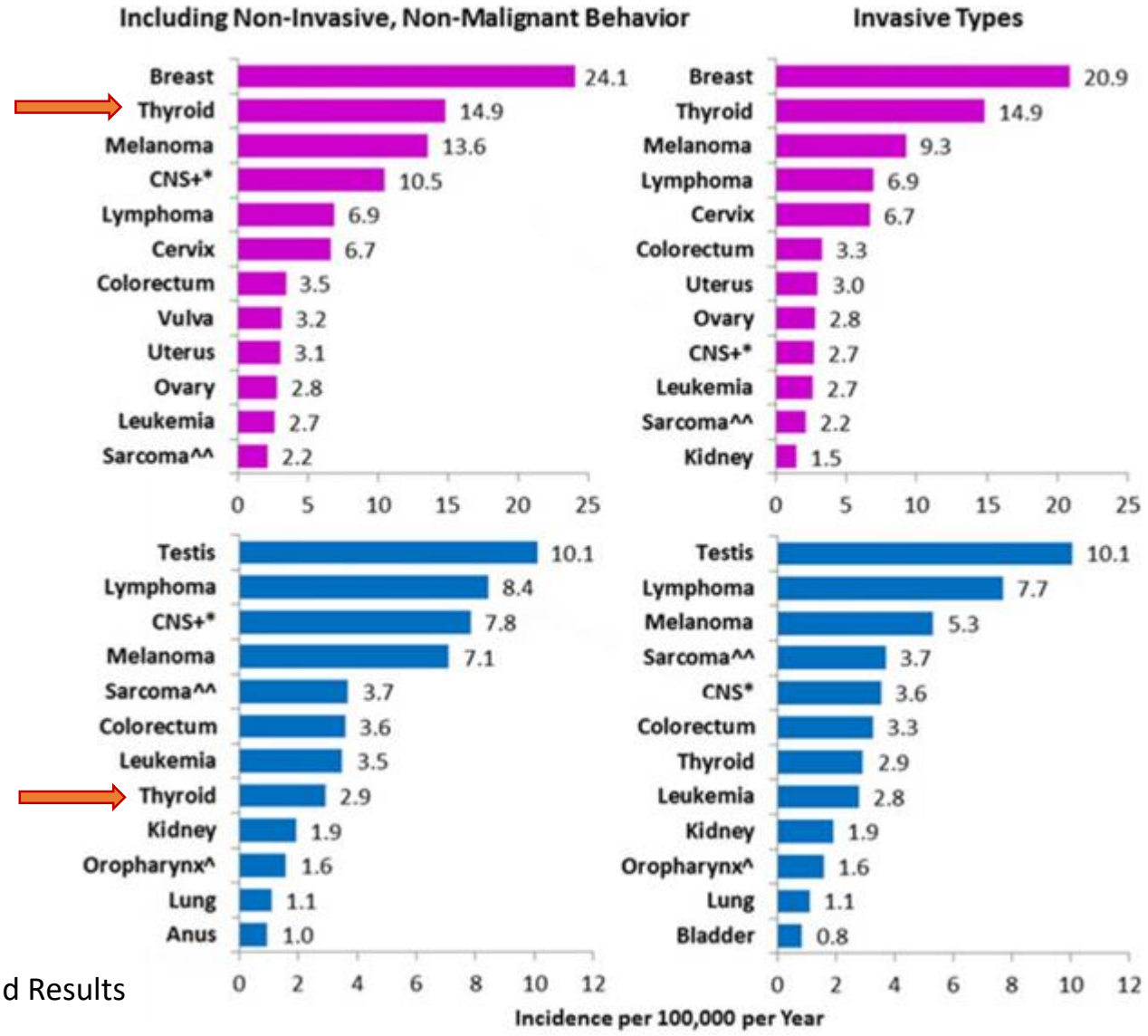
Table 4 – Age-standardised incidence (*I*) and mortality (*M*) rates of the most frequent cancer types in women aged 15-to-44 years in more developed and less developed countries (GLOBOCAN).

Cancer	No of new cancers	Age-standardised incidence rate (per 100,000)	Age-standardised mortality rate (per 100,000)	I/M ratio
a) More developed countries				
Breast	78,001	27.7	4.1	7
Thyroid	26,251	10.1	0.0[a]	203
Cervix uteri	25,638	9.7	1.9	5
Melanoma of skin	20,675	7.9	0.5	14
Ovary	11,105	4.1	1.0	4
Colorectum	10,896	3.9	1.1	4
b) Less developed countries				
Breast	207,679	16.1	4.3	4
Cervix uteri	152,496	11.8	3.8	3
Thyroid	36,282	2.8	0.1	19
Ovary	35,381	2.7	1.1	3
Leukaemia	30,735	2.4	1.9	1
Colorectum	29,076	2.3	1.1	2

a Corresponding to an estimate of 129 deaths.

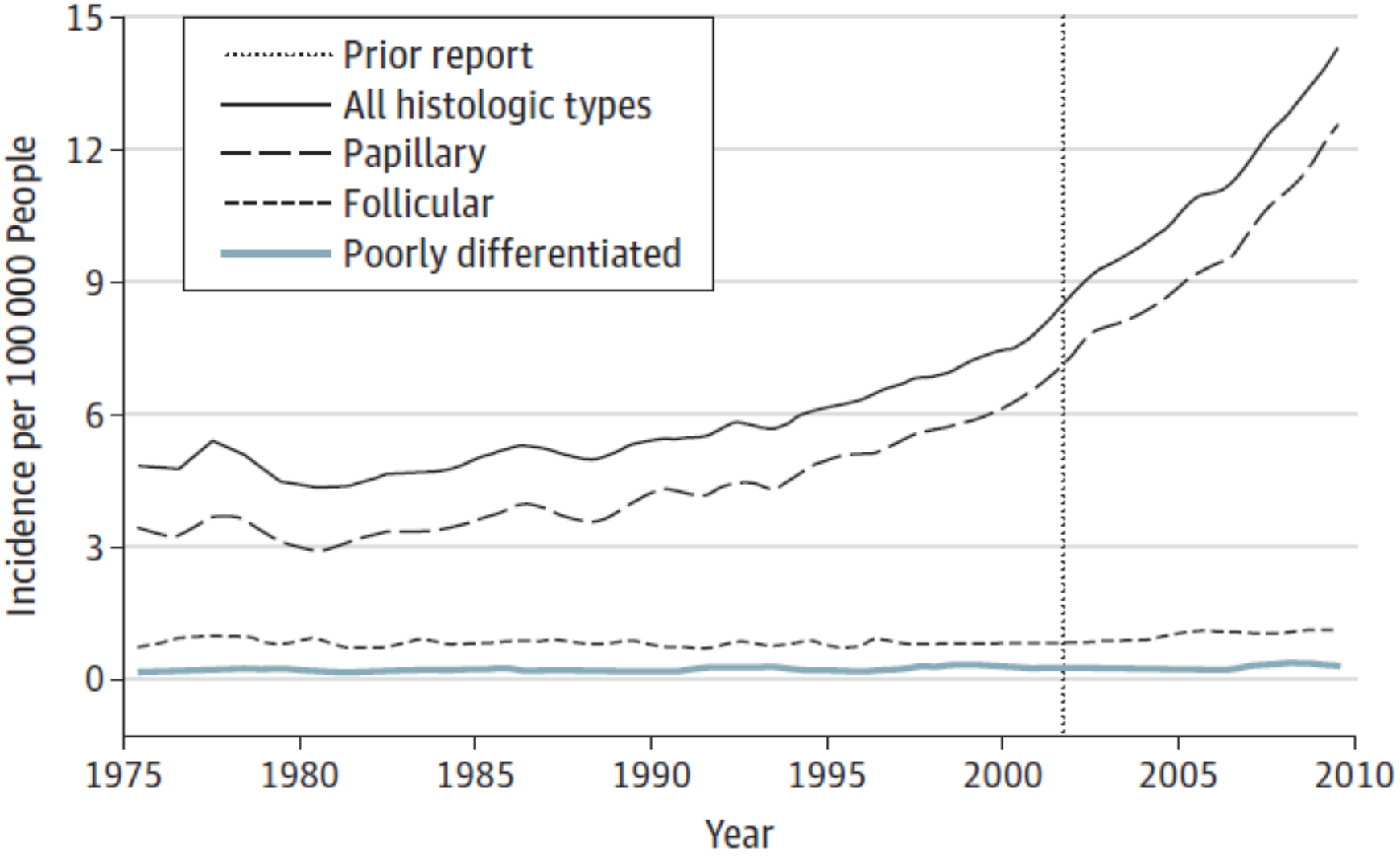
Franceschi & Wild, 2013

Incidence of the 12 most frequent cancers is illustrated in adolescents and young adults (AYAs) ages 15 to 39 years of age from 2004 through 2009

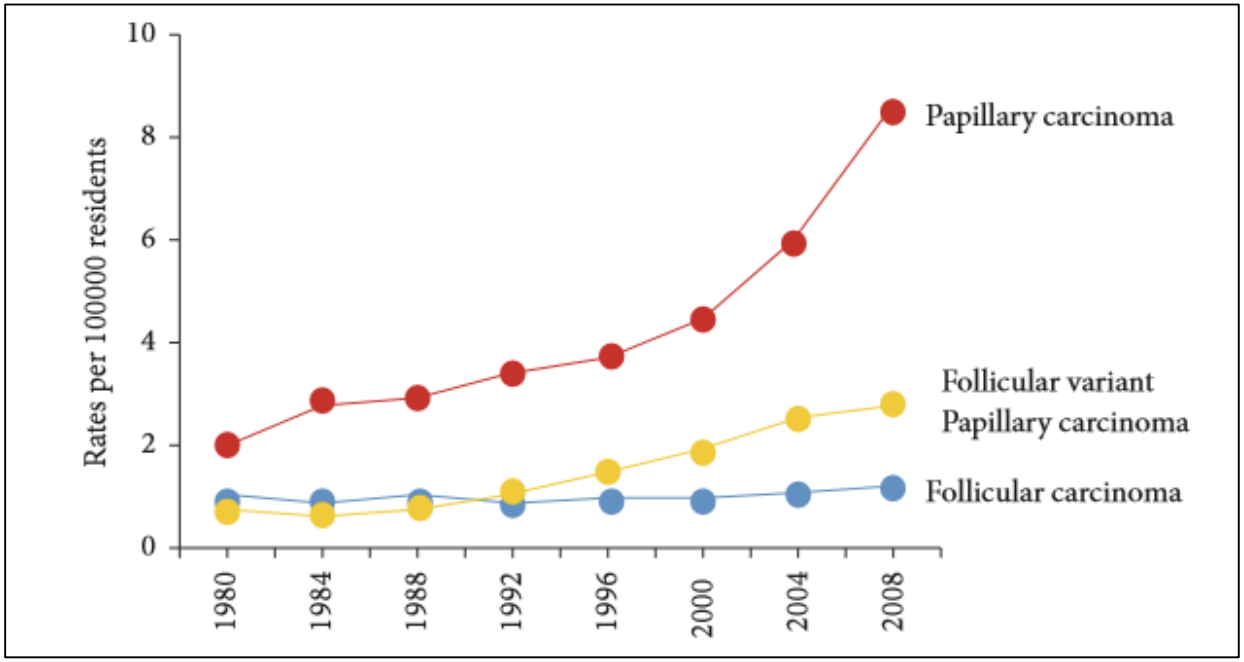


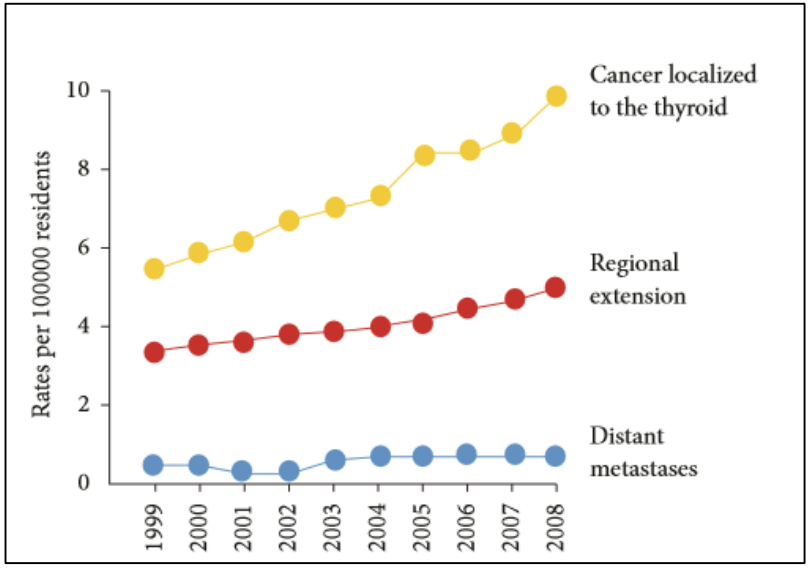
Surveillance, Epidemiology, and End Results [SEER] 18 registries

Incidenza annuale per istotipo

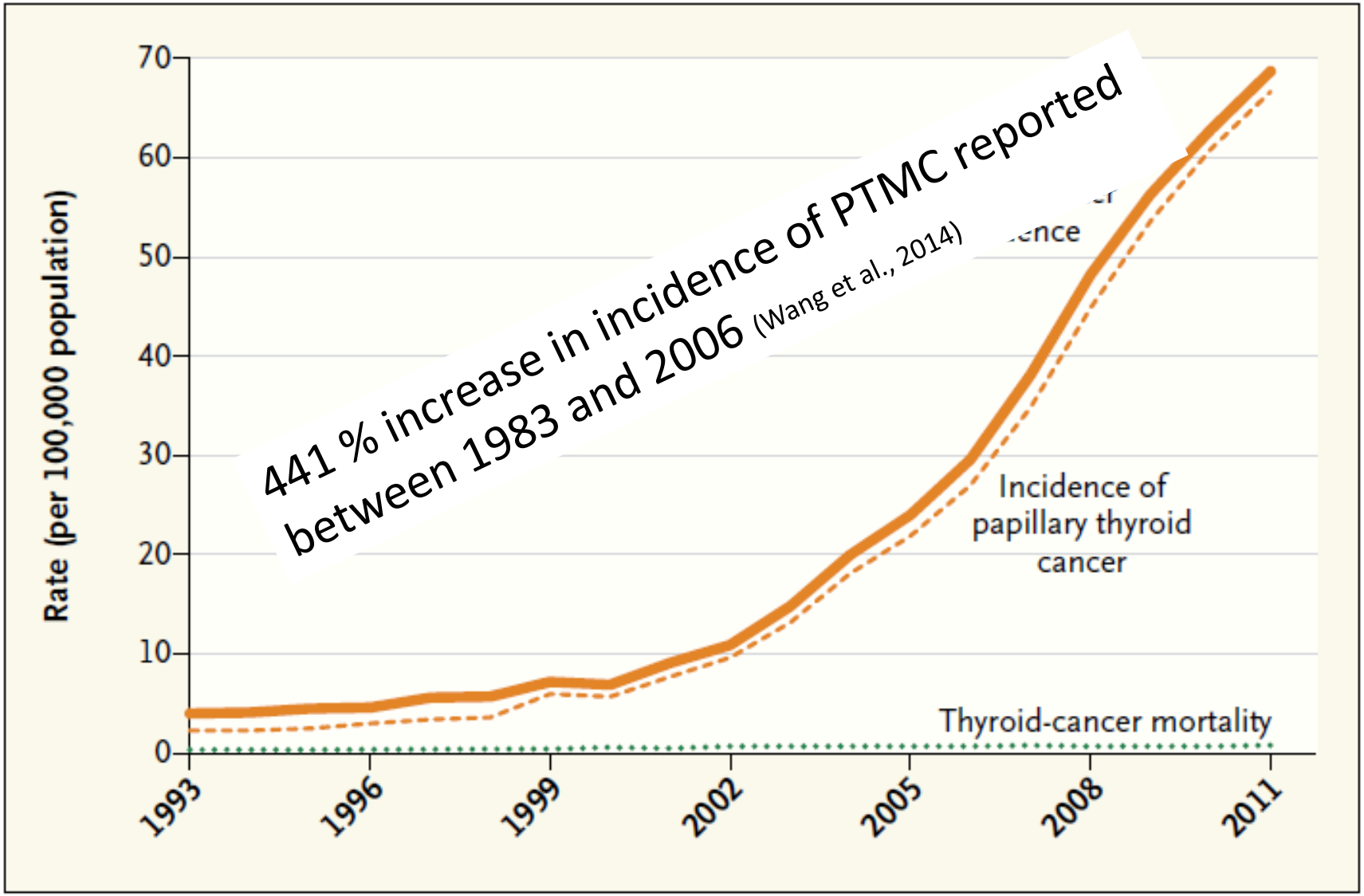


Davies & Welch, 2014





Pellegriti et al., 2013



Ahn et al., 2014; Davies & Welch, 2014

L'incidenza di cancro della tiroide è in significativo aumento in tutto il mondo: possibili ragioni

L'aumento è apparente (non più cancri, ma più diagnosi)

- Ampia diffusione di procedure diagnostiche (ecografia e citologia su agoaspirato)
- L'aumento di incidenza riguarda prevalentemente i microcarcinomi
- L'aumentata diagnosi di microcarcinomi incidentali è dovuta a:
  -le tiroidectomie totale per le lesioni benigne sono più frequenti
  -gli esami istopatologici sono più dettagliati
  -la scoperta incidentale di noduli tiroidei durante altri accertamenti sono più frequenti
- Era già nota la elevata frequenza di piccoli cancri tiroidei non noti come reperto autoptico
- Migliore accuratezza dei Registri

L'aumento è reale (più cancri per variazione fattori di rischio)

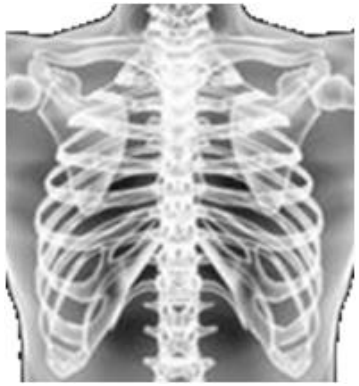
- Sono aumentati anche i tumori grossi
- L'incidenza dei tumori grossi non si è ridotta, come ci si attenderebbe da diagnosi più precoce
- Solo il carcinoma papillare è aumentato
- La migliore accuratezza dei registri avrebbe portato ad aumenti incidenza anche per altri tumori

Modificato da Pellegriti et al., 2013

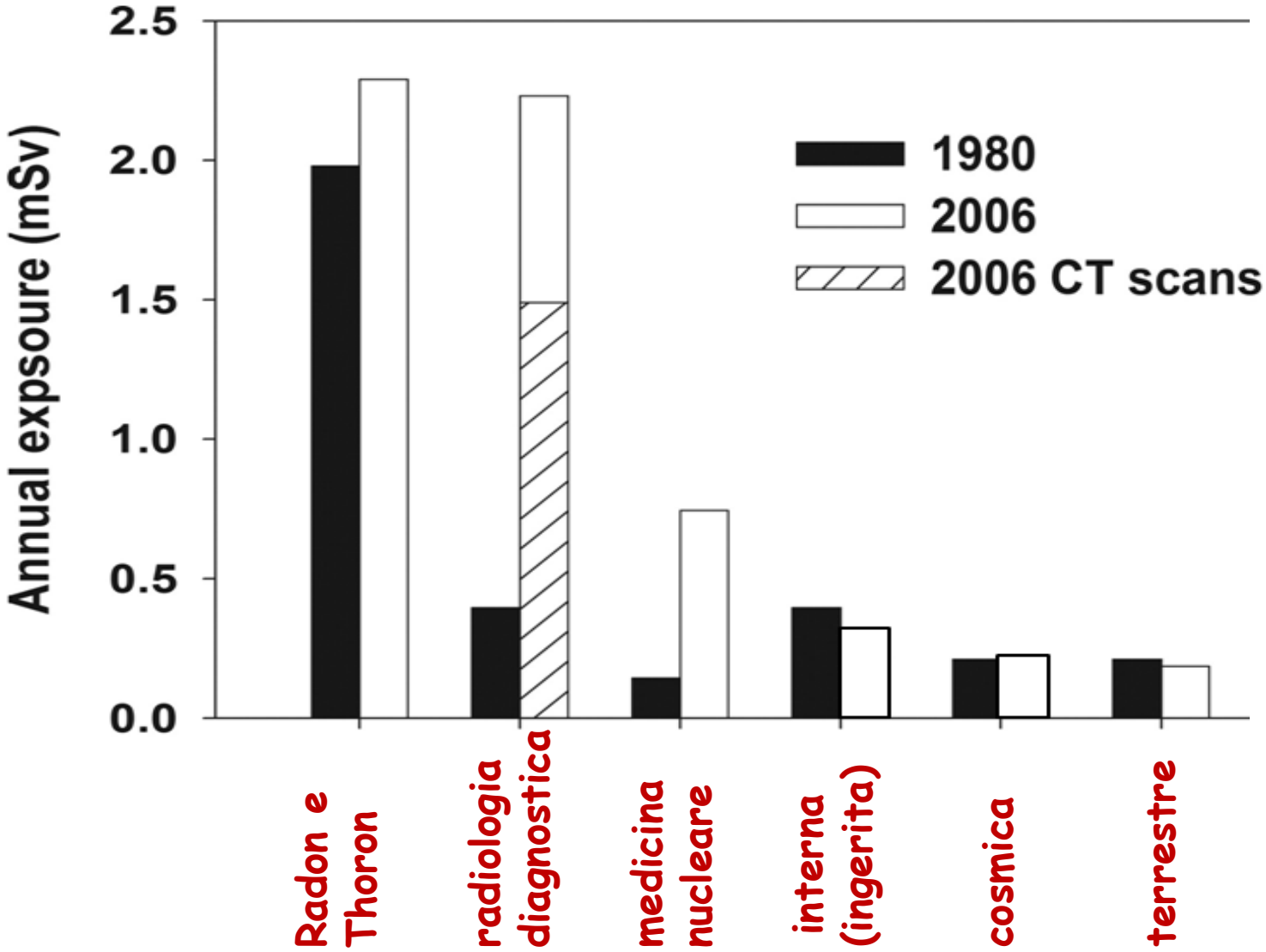
Table 3: Potential carcinogenic factors thyroid cancer.

	Factor	Source
Exogenous	X-rays	Medical imaging (dental X-ray and CT scans)
	^{131}I	Nuclear medicine procedures
	Iodine	Diet, iodine prophylaxis, $BRAF^{V600E}$ (?)
	Nitrate	Water and diet
	Westernized lifestyle and environmental	Undiscovered carcinogens
	pollutants	Bisphenol A (BPA), polychlorinated biphenyls (PCB), polybrominated diphenyl ethers (PBDEs)
	Factor	Mechanism
Endogenous	TSH	Thyroid growth stimulation
	Autoimmune	increased TSH and oxidative stress
	Thyroiditis	
	Obesity and insulin resistance	Hyperinsulinemia promotes cancer, but this factor is not specific for the thyroid

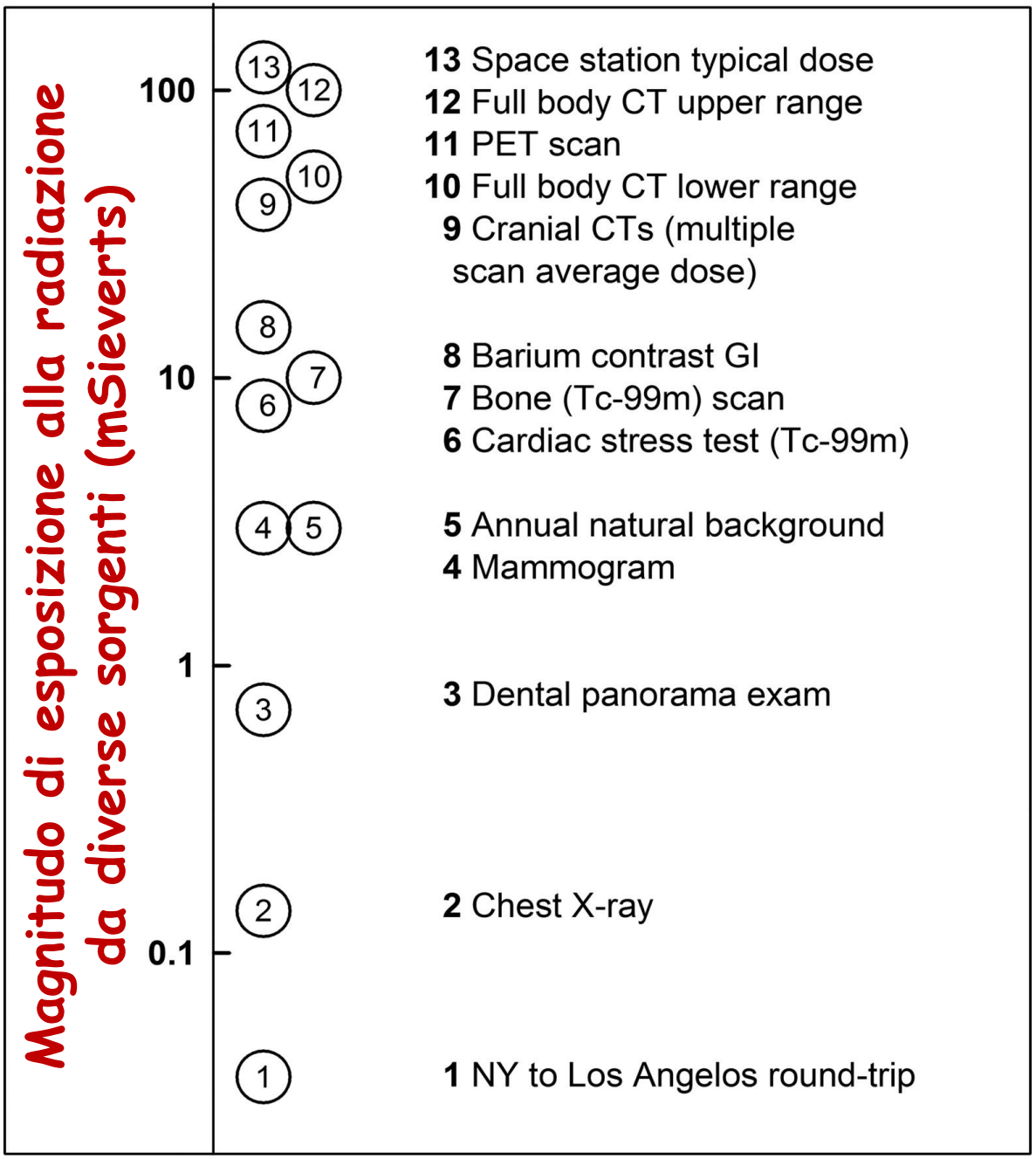
Aumentata radiazione

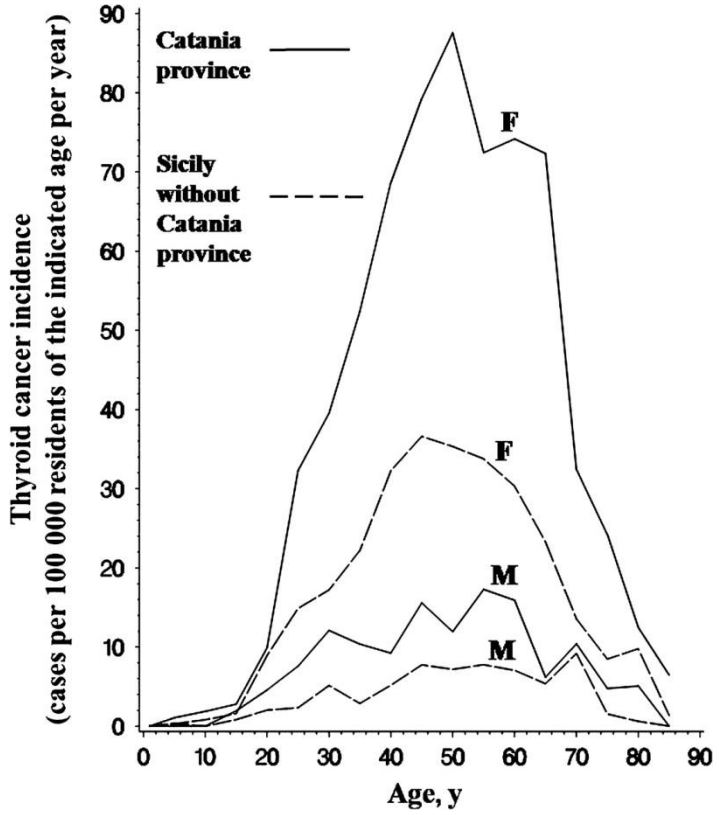


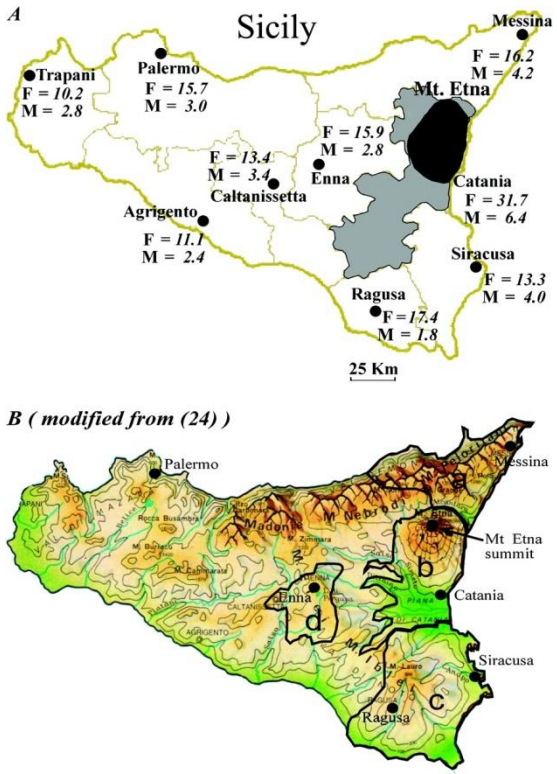
Fonti di esposizione a radiazioni



Sinnott et al., Endocr Rev 2010


Magnitudo di esposizione alla radiazione da diverse sorgenti (mSieverts)
100
10
1
0.1
13 Space station typical dose
12 Full body CT upper range
11 PET scan
10 Full body CT lower range
9 Cranial CTs (multiple scan average dose)
8 Barium contrast GI
7 Bone (Tc-99m) scan
6 Cardiac stress test (Tc-99m)
5 Annual natural background
4 Mammogram
3 Dental panorama exam
2 Chest X-ray
1 NY to Los Angelos round-trip





Element	MAC (µg/L)	No. of specimens with concentrations greater than MAC/total No. (maximum value measured)		
		Catania	Palermo	Ragusa
Boron (B)	1000	131/478 (2100)	0/151 (750)	0/73 (218)
Iron (Fe)	200	92/280 (5300)	6/153 (1380)	1/92 (1330)
Manganese (Mn)	50	87/264 (2600)	3/151 (138)	0/92 (14)
Vanadium (V)	50	193/280 (179)	0/142 (<7)	0/73 (20)
^{222}Radon (^{222}Rn)†	11	48/119 (57)	–	–

Pellegriti et al, J Natl Cancer Inst 2009

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PERSPECTIVE

Korea's Thyroid-Cancer "Epidemic" — Screening and Overdiagnosis

Hyeong Sik Ahn, M.D., Ph.D., Hyun Jung Kim, M.P.H., Ph.D., and H. Gilbert Welch, M.D., M.P.H.
N Engl J Med 2014; 371:1765-1767 | November 6, 2014 | DOI: 10.1056/NEJMp1409841

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What caused jump in thyroid cancer cases?

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TTS Service will resume in two weeks

By Jung Min-ho, Jung Sung-eun

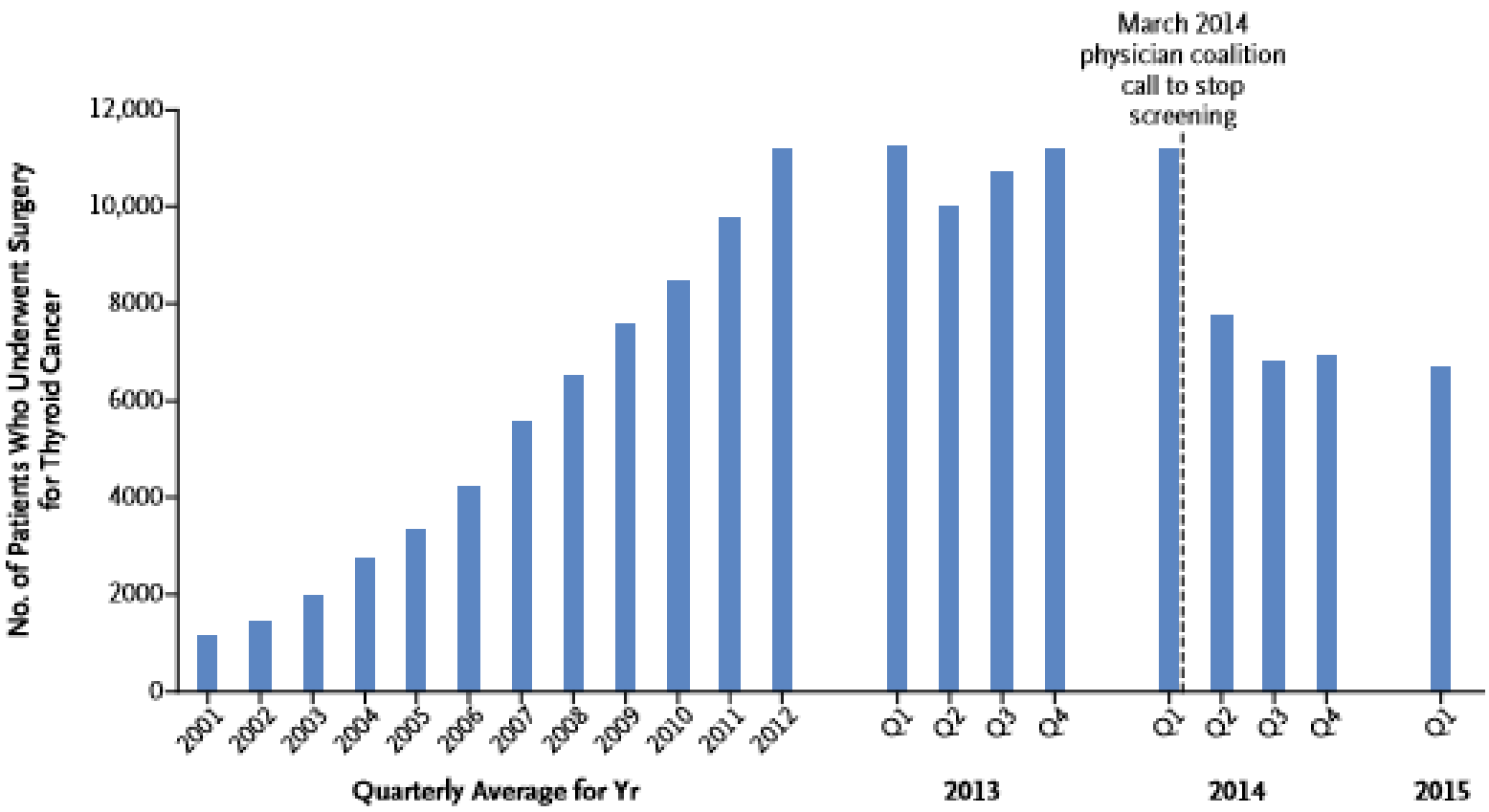


Figure 1. Trend in the Number of Operations for Thyroid Cancer in South Korea, 2001–2015.

Data are from the Health Insurance Review and Assessment Service, South Korea.

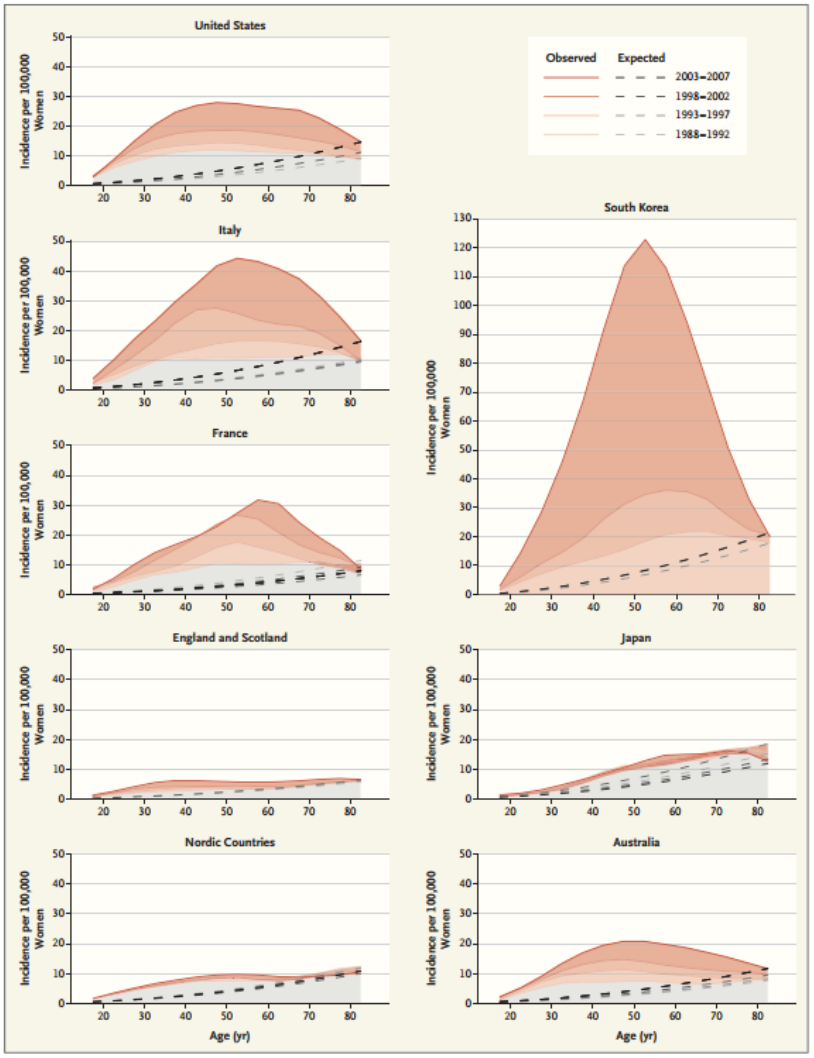
Ahn HS, and Welch HG, NEJM 2015

Worldwide Thyroid-Cancer Epidemic? The Increasing Impact of Overdiagnosis

Salvatore Vaccarella, Ph.D., Silvia Franceschi, M.D., Freddie Bray, Ph.D., Christopher P. Wild, Ph.D., Martyn Plummer, Ph.D., and Luigino Dal Maso, Ph.D.

Several reports have described dramatic increases over recent decades in the incidence of thyroid cancer,[1] predominantly small papillary carcinomas,[2] even as thyroid-cancer–related mortality rates have not changed substantially.[3] The largest increase has been observed in South Korea: the incidence among people 15 to 79 years of age (standardized to the world population) increased from 12.2 cases per 100,000 persons in 1993–1997 to 59.9 cases per 100,000 persons in 2003–2007,[1] making thyroid cancer the most commonly diagnosed cancer among women in that country.

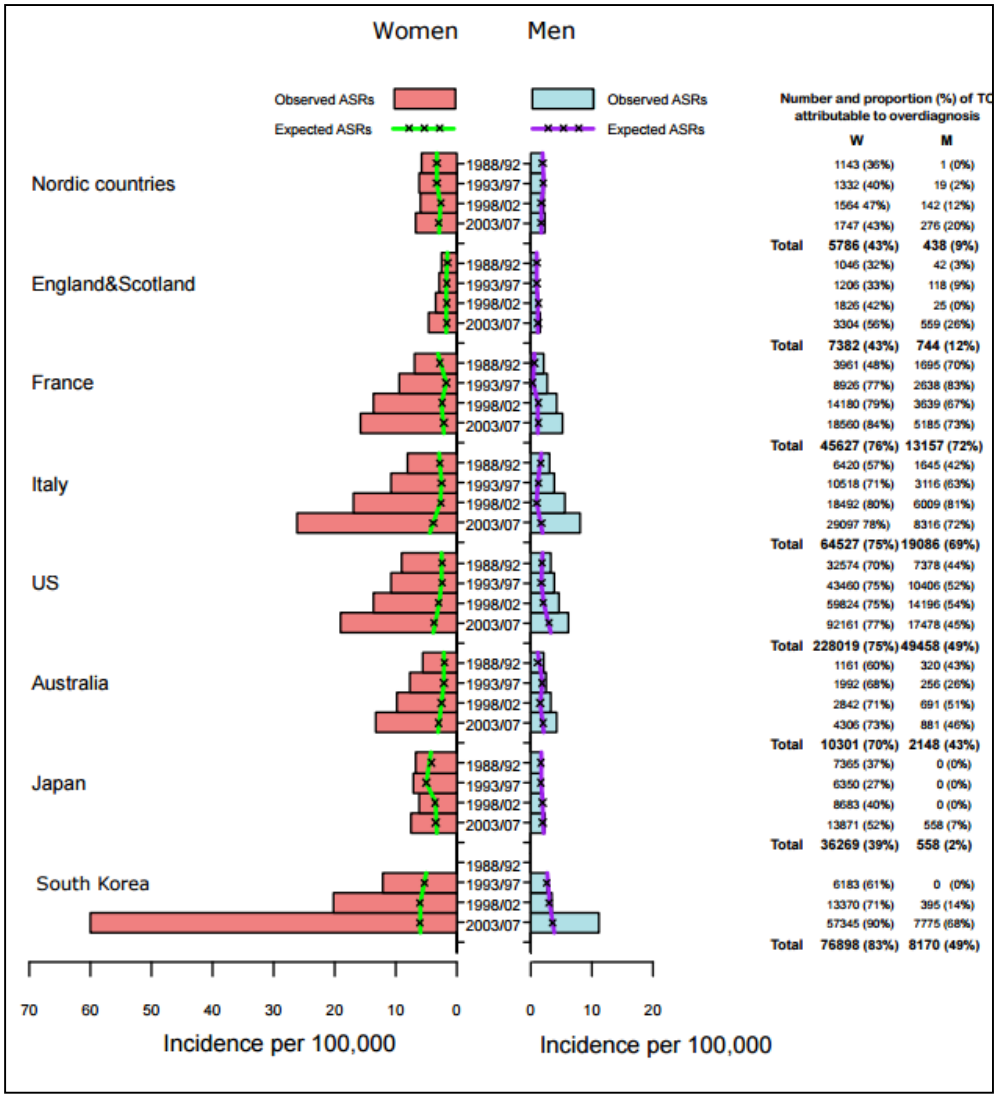
The introduction of new diagnostic techniques (ultrasonography, computed tomography, and magnetic resonance imaging), combined with increased medical surveillance and access to health care services, can lead to massive increases in detection of small papillary lesions caused by the



Approximately 228,000 cases diagnosed in women in the United States between 1988 and 2007 would be considered overdiagnoses . Corresponding numbers are 65,000 in Italy, 46,000 in France, and 36,000 in Japan.
Among South Korean women, overdiagnosis accounted for approximately 77,000 extra cases of thyroid cancer between 1993 and 2007

The number of overdiagnoses was smaller but still substantial in Australia (10,000), England and Scotland (7000), and the Nordic countries (Denmark, Finland, Norway, and Sweden; 6000)

Overall, we estimate that more than 470,000 women and 90,000 men may have been overdiagnosed with thyroid cancer over two decades in these 12 countries, with steady incremental increases over time and little evidence of stabilization.



Number and proportion (%) of TC attributable to overdiagnosis	W	M
	1143 (36%)	1 (0%)
	1332 (40%)	19 (2%)
	1564 47%)	142 (12%)
	1747 (43%)	276 (20%)
Total	**5786 (43%)**	**438 (9%)**
	1046 (32%)	42 (3%)
	1206 (33%)	118 (9%)
	1826 (42%)	25 (0%)
	3304 (56%)	559 (26%)
Total	**7382 (43%)**	**744 (12%)**
	3961 (48%)	1695 (70%)
	8926 (77%)	2638 (83%)
	14180 (79%)	3639 (67%)
	18560 (84%)	5185 (73%)
Total	**45627 (76%)**	**13157 (72%)**
	6420 (57%)	1645 (42%)
	10518 (71%)	3116 (63%)
	18492 (80%)	6009 (81%)
	29097 78%)	8316 (72%)
Total	**64527 (75%)**	**19086 (69%)**
	32574 (70%)	7378 (44%)
	43460 (75%)	10406 (52%)
	59824 (75%)	14196 (54%)
	92161 (77%)	17478 (45%)
Total	**228019 (75%)**	**49458 (49%)**
	1161 (60%)	320 (43%)
	1992 (68%)	256 (26%)
	2842 (71%)	691 (51%)
	4306 (73%)	881 (46%)
Total	**10301 (70%)**	**2148 (43%)**
	7365 (37%)	0 (0%)
	6350 (27%)	0 (0%)
	8683 (40%)	0 (0%)
	13871 (52%)	558 (7%)
Total	**36269 (39%)**	**558 (2%)**
	6183 (61%)	0 (0%)
	13370 (71%)	395 (14%)
	57345 (90%)	7775 (68%)
Total	**76898 (83%)**	**8170 (49%)**

Vaccarella et al., NEJM 2016

Thyroid papillary microcarcinoma

≤ 1 cm

clinically evident or not, with or without extrathyroidal extension, unifocal o multifocal

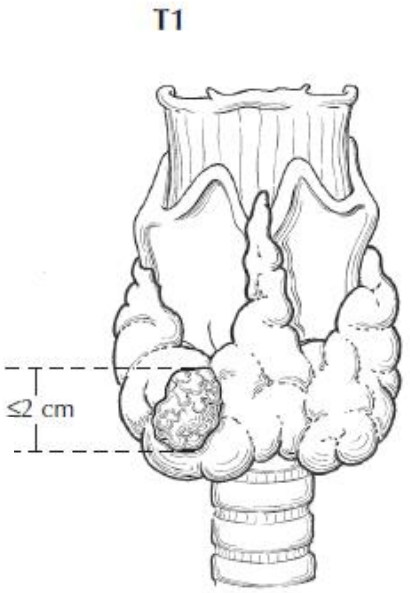
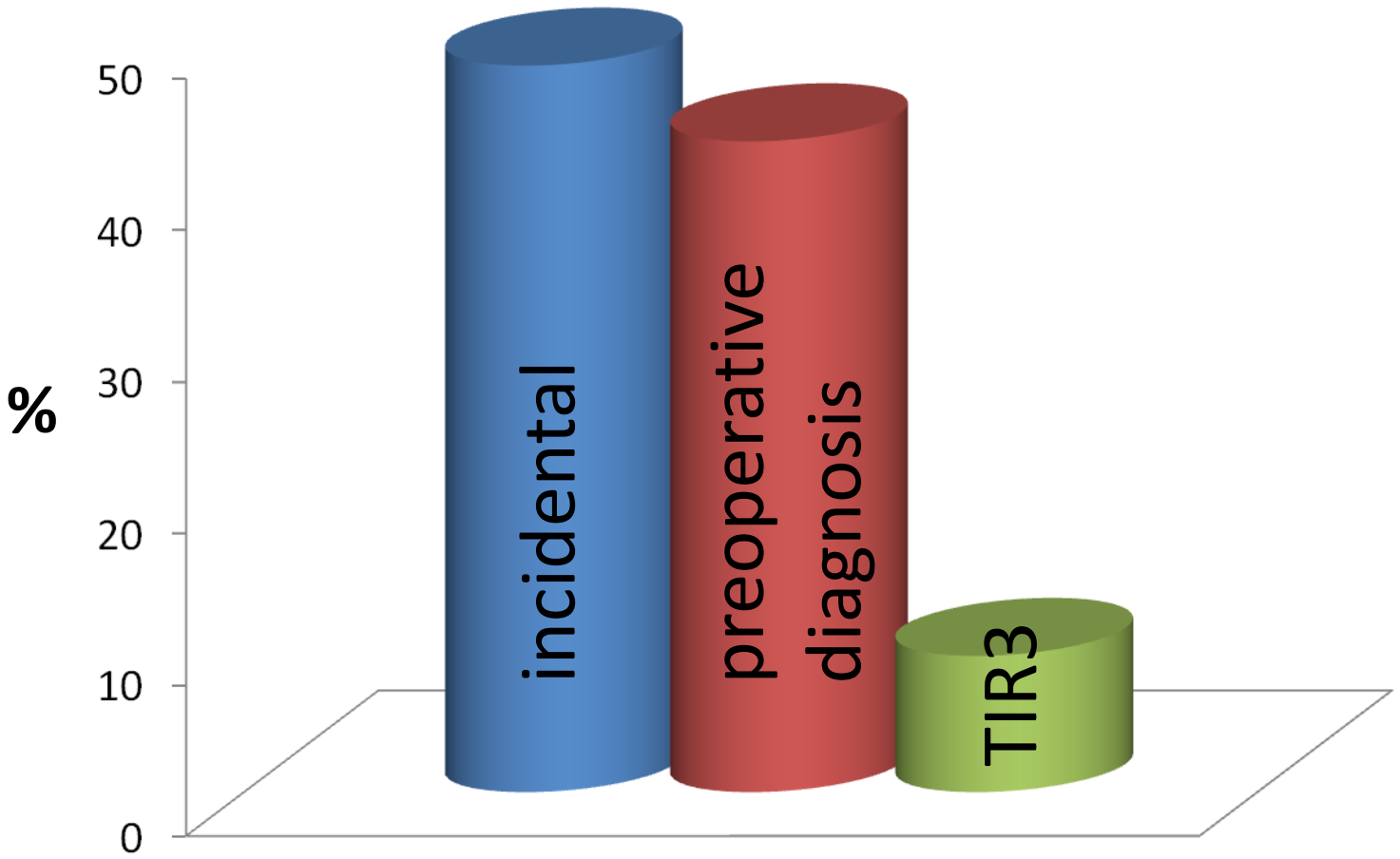


FIGURE 8.2. T1 is defined as tumor 2 cm or less in greatest dimension limited to the thyroid.

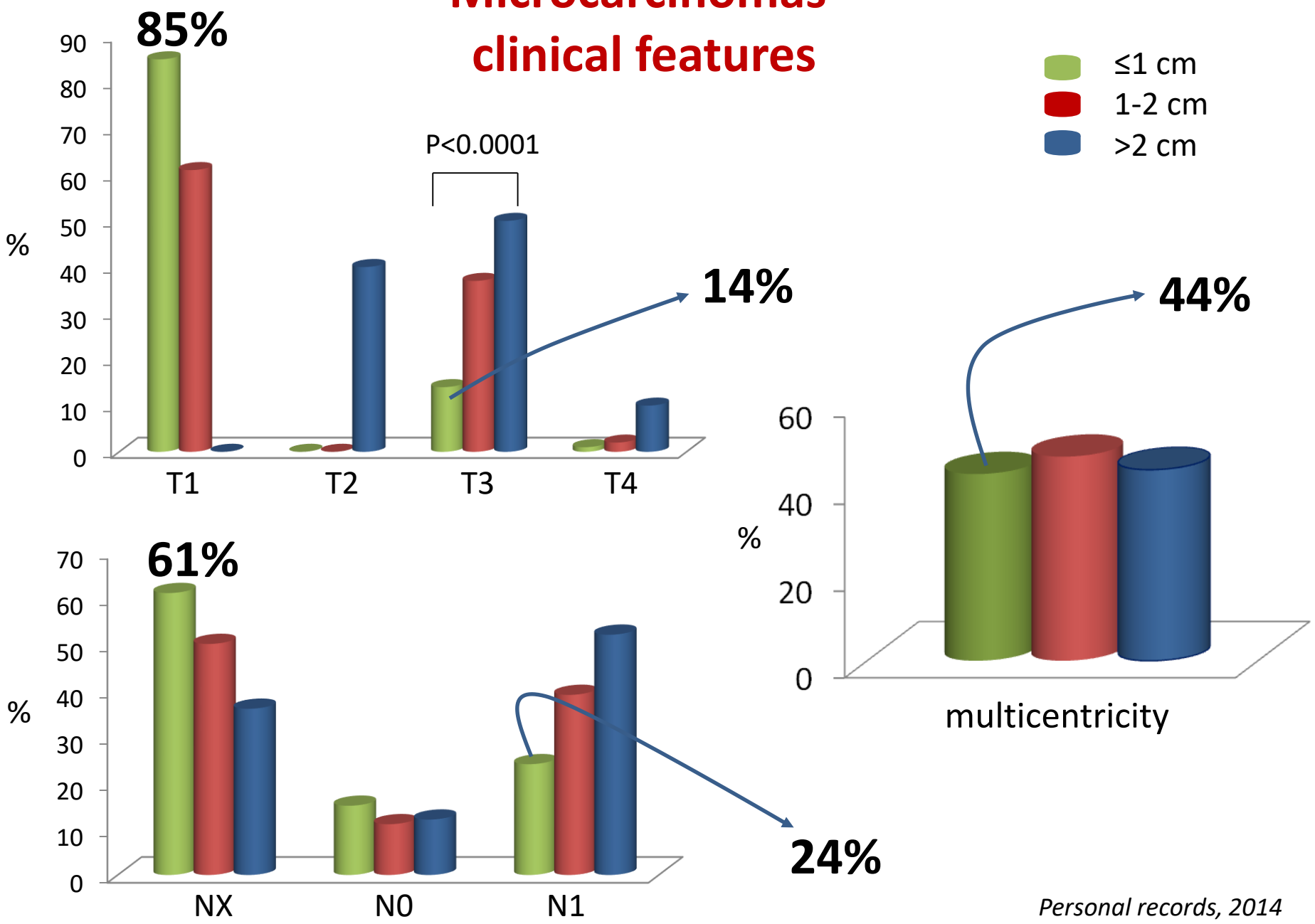
Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, et al. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer-Verlag; 2010

Papillary microcarcinomas: diagnosis



Personal records, 2014

Microcarcinomas clinical features



Personal records, 2014

Microcarcinomas: clinical features

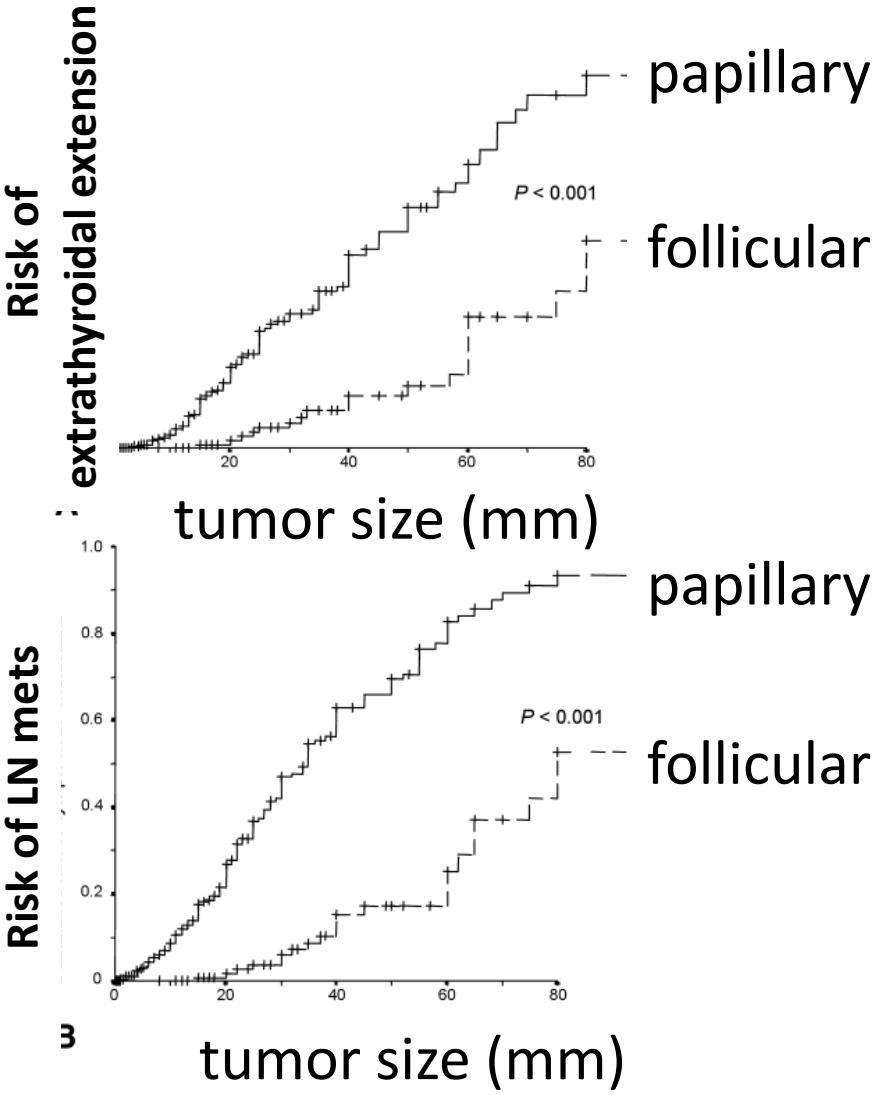
Table 3
Pathological features of mPTC in different series.

Authors (ref)	Year	Series	Multicentricity	Bilaterality	Extrathyroidal invasion	Lymphnode metastases	Distant metastases
Baudin et al[46]	1998	281	112 (40%)	46 (16%)	42 (15%)	121 (43%)	8 (3%)
Hay et al[47]	1992	535	107 (20%)	54 (10%)	10 (2%)	172 (32%)	1 (0.2%)
Roti et al[48]	2006	243	78 (32%)	45 (19%)	42 (17%)	32 (13%)	4 (1.6%)
Chow et al[49]	2003	203	63 (31%)	–	42 (20.7%)	50 (24.6%)	2 (1.0%)
Ito et al[50]	2003	626	269 (42.8%)	–	10 (1.6%)	300 (50.5%)	0 (0%)
Noguchi et al[51]	1996	867	48 (5.5%)	44 (5%)	72 (8.3%)	75 (8.6%)	0 (0%)

Mean **11 %** **28%**

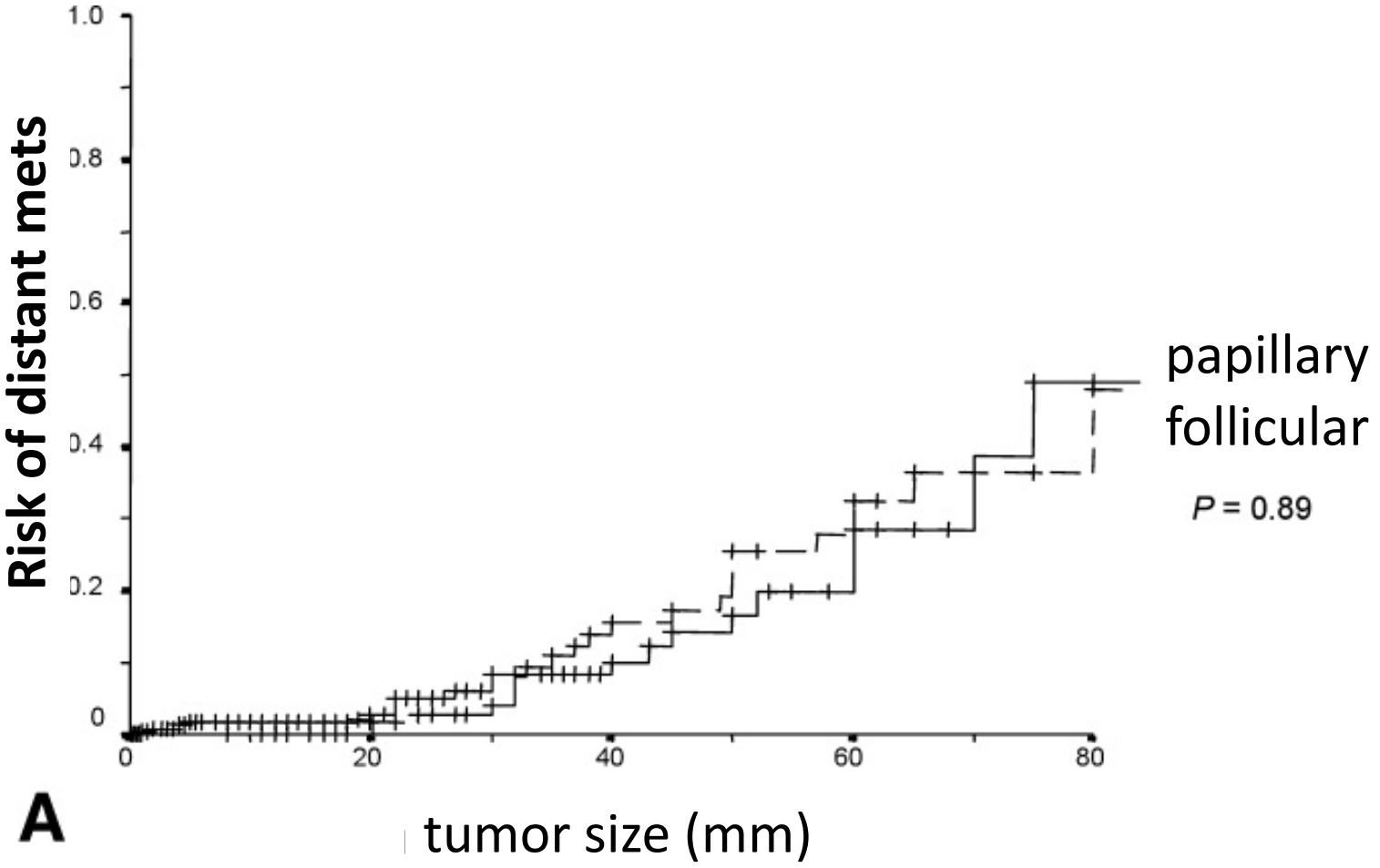
Pacini, 2012

microcarcinoma
tumor size as a risk factor



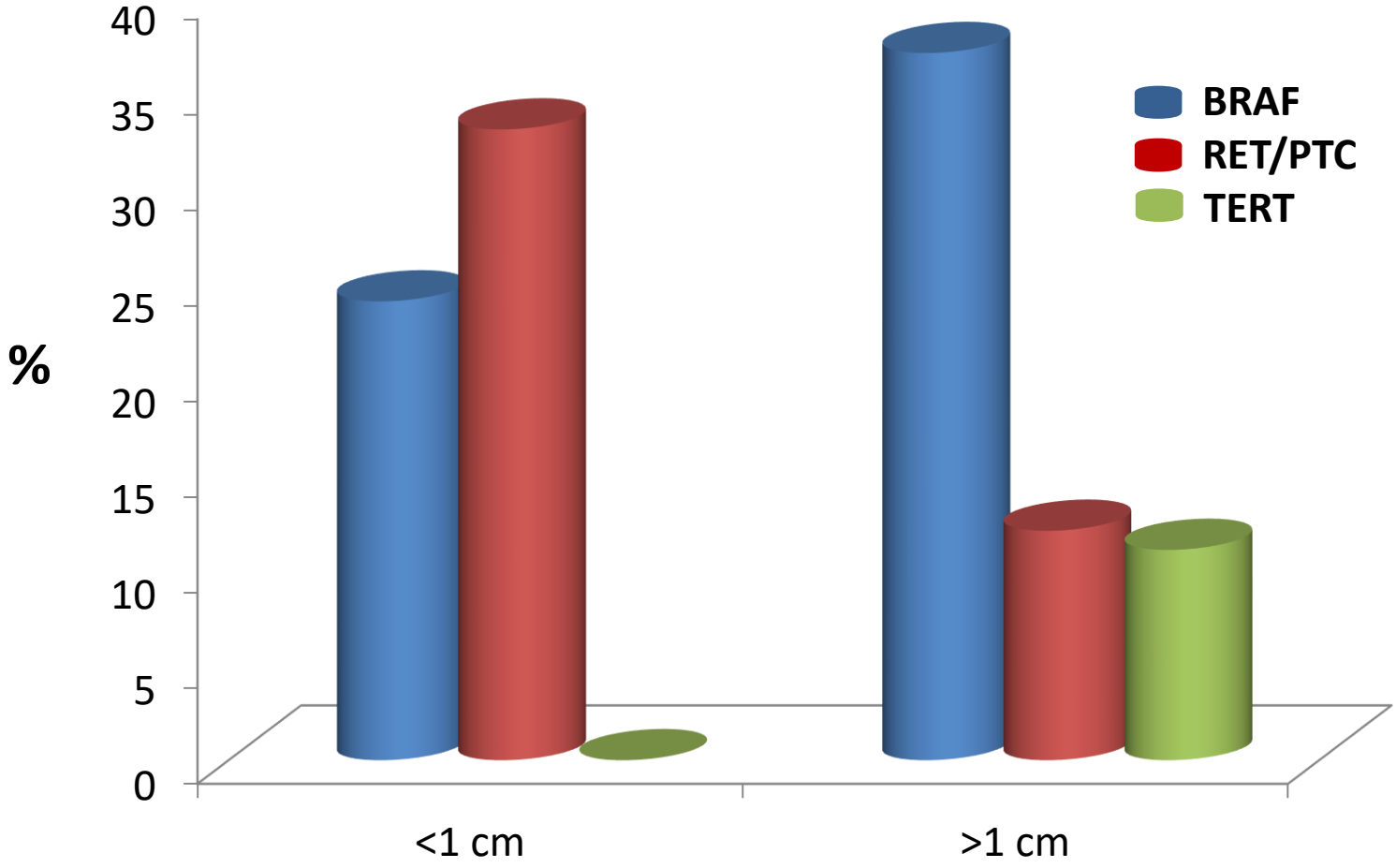
Machens, 2004

microcarcinoma
tumor size as a risk factor



Machens, 2004

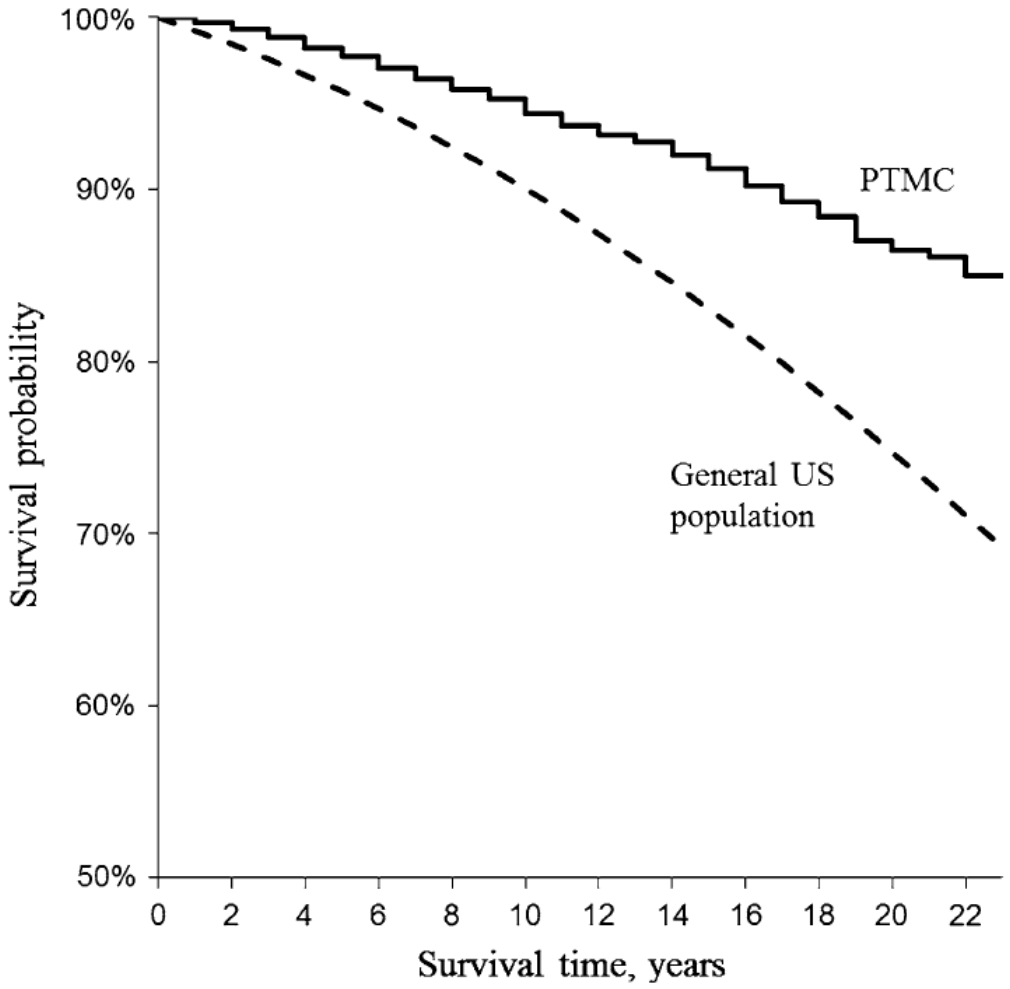
Genetic background of papillary microcarcinoma



Personal records, 2014

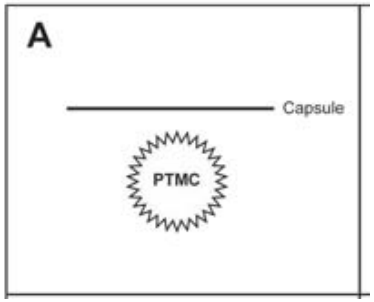
PTMC: excellent prognosis

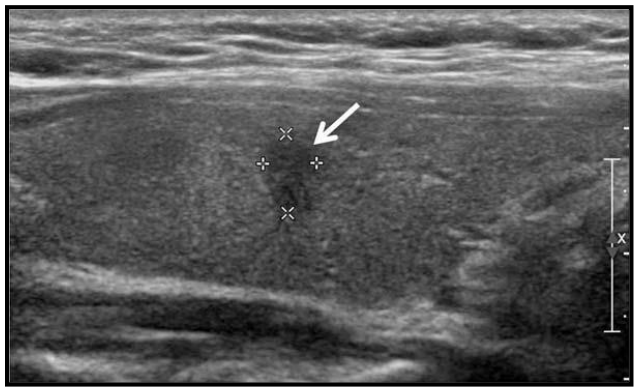
29,512 patients with PTC <1 cm (PTMC) identified in the SEER database between 1988 and 2010



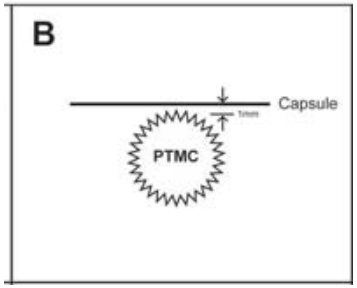
Wang et al, World J Surg 2014

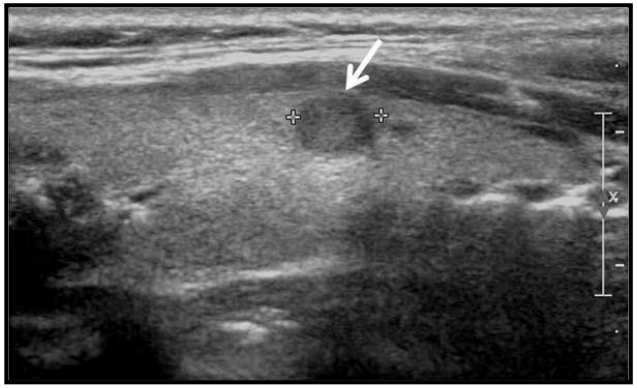
Terapia: l'importanza della sede



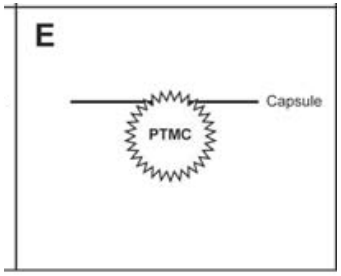


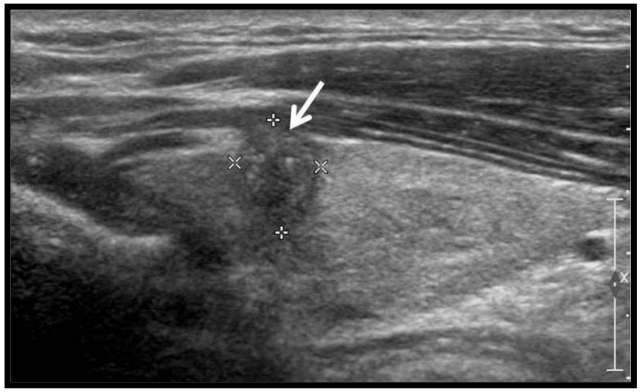
Intrathyroidal
small focus





Intrathyroidal small
focus, adjacent to
the capsule

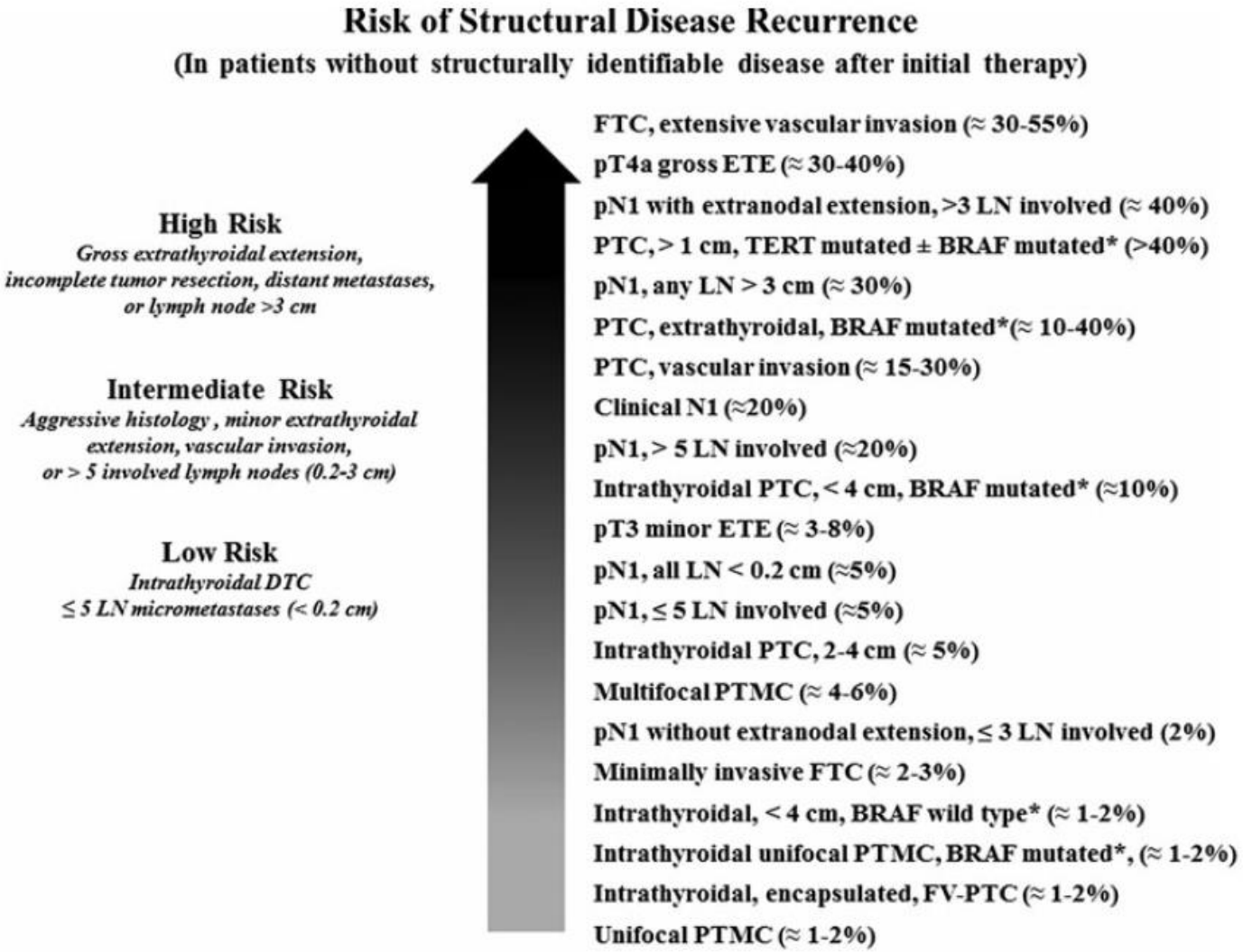




Perithyroidal
fat invasion

Moon et al., Endocr Pract 2014

2015 ATA Guidelines, Haugen et al, Thyroid 2016
Cosa cambia?



Low

NO

Low to intermediate

conflicting

High

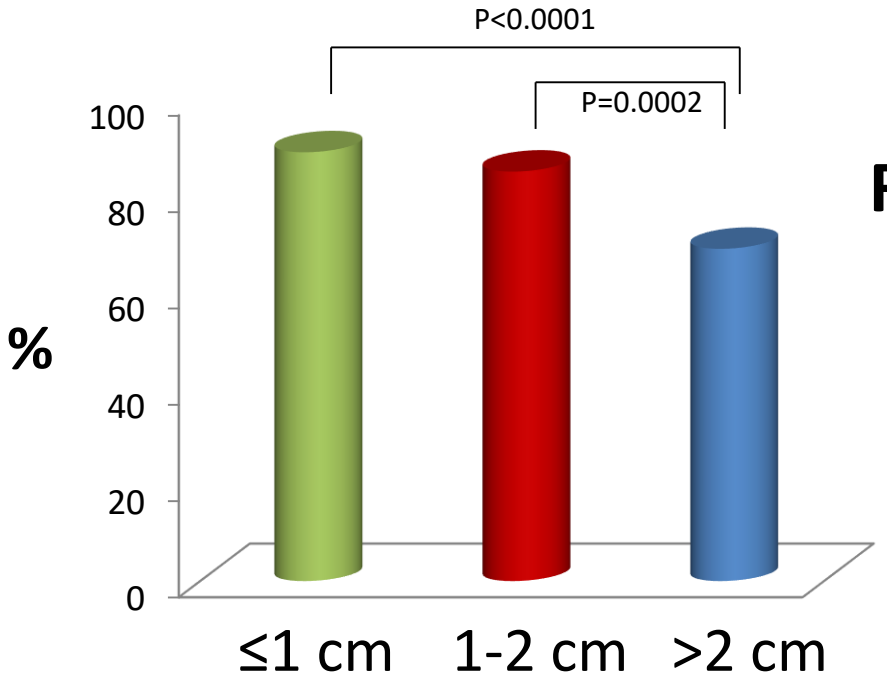
YES

Table 14. Characteristics According to the American Thyroid Association Risk Stratification System and AJCC/TNM Staging System That May Impact Postoperative Radioiodine Decision-Making

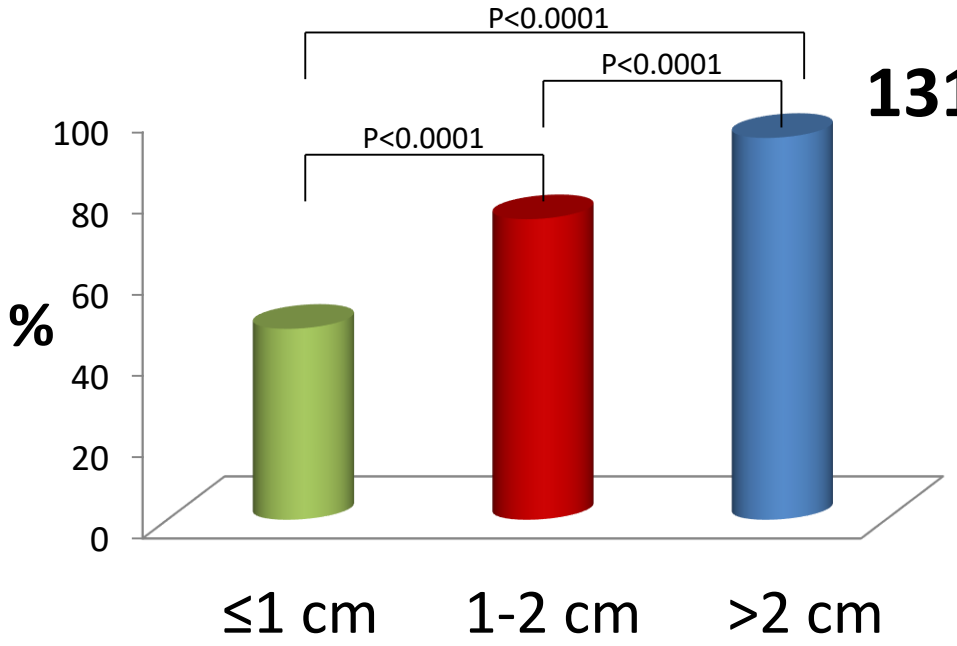
ATA risk Staging (TNM)	*Description*	*Body of evidence suggests RAI improves disease-specific survival?*	*Body of evidence suggests RAI improves disease-free survival?*	*Postsurgical RAI indicated?*
ATA low risk T1a N0,Nx M0,Mx	Tumor size ≤1 cm (uni-or multi-focal)	No	No	No
ATA low risk T1b,T2 N0, Nx M0,Mx	Tumor size >1–4 cm	No	Conflicting observational data	Not routine[b]—May be considered for patients with aggressive histology or vascular invasion (ATA intermediate risk).
ATA low to intermediate risk T3 N0,Nx M0,Mx	Tumor size >4 cm	Conflicting data	Conflicting observational data	Consider[b]—Need to consider presence of other adverse features. Advancing age may favor RAI use in some cases, but specific age and tumor size cutoffs subject to some uncertainty.[a]
ATA low to intermediate risk T3 N0,Nx M0,Mx	Microscopic ETE, any tumor size	No	Conflicting observational data	Consider[b]—Generally favored based on risk of recurrent disease. Smaller tumors with microscopic ETE may not require RAI.
ATA low to intermediate risk T1-3 N1a M0,Mx	Central compartment neck lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age (NTCTCSG Stage III)	Conflicting observational data	Consider[b]—Generally favored, due to somewhat higher risk of persistent or recurrent disease, especially with increasing number of large (>2–3 cm) or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.[a] However, there is insufficient data to mandate RAI use in patients with few (<5) microscopic nodal metastases in central compartment in absence of other adverse features.
ATA low to intermediate risk T1-3 N1b M0,Mx	Lateral neck or mediastinal lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age	Conflicting observational data	Consider[b]—Generally favored, due to higher risk of persistent or recurrent disease, especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.[a]
ATA high risk T4 Any N Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
ATA high risk M1 Any T Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

2015 ATA Guidelines, Haugen et al, Thyroid 2016

Microcarcinomas: better prognosis… even if less treated!



Remission



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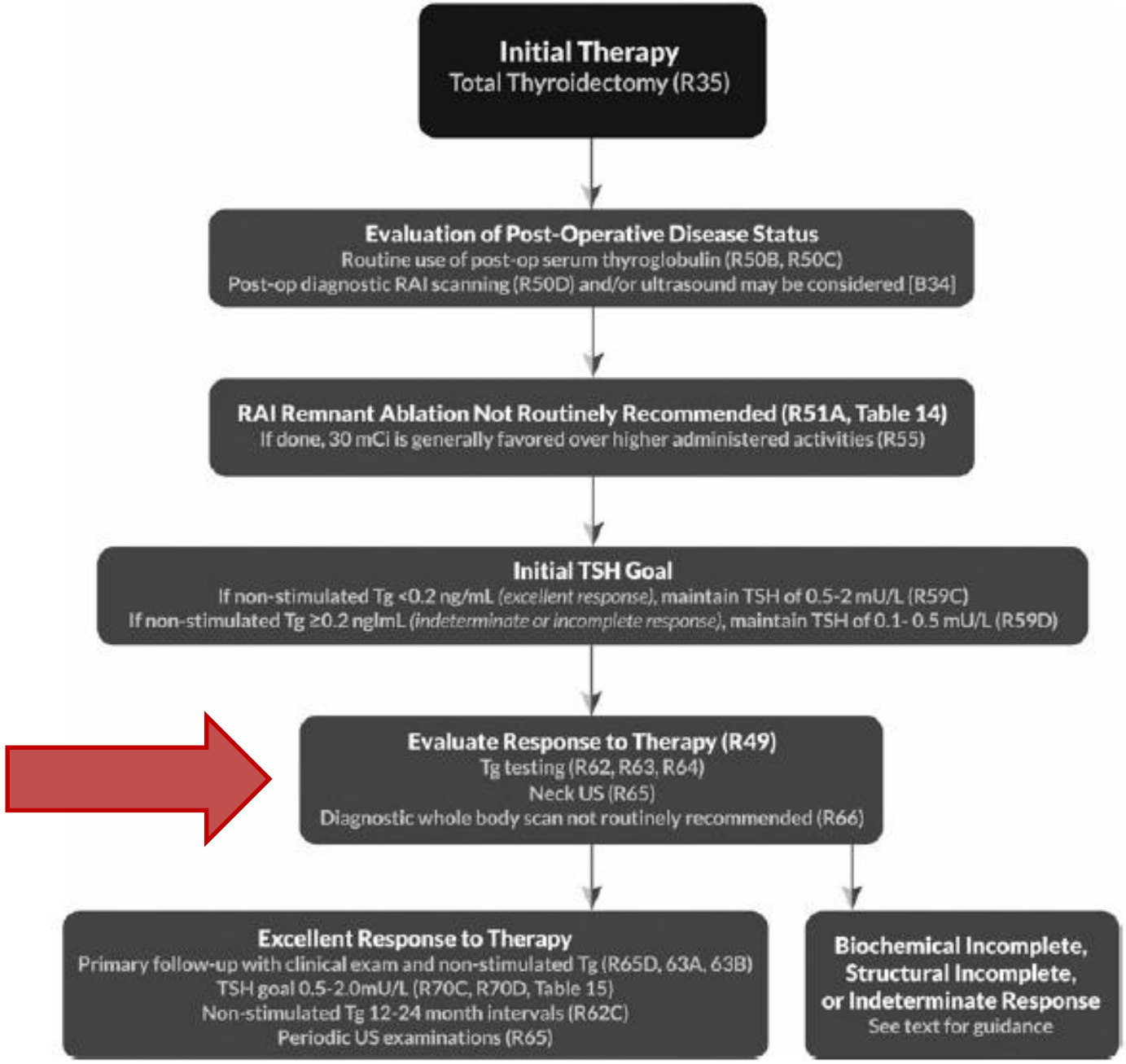


2015 ATA Guidelines, Haugen et al, Thyroid 2016

Excellent response: *No clinical, biochemical or structural evidence of disease.*	Nonstimulated Tg < 0.2 ng/mL or Stimulated Tg < 2 ng/mL and Undetectable TgAb and Negative imaging
Biochemical incomplete response: *Abnormally elevated serum Tg or rising TgAb levels in the absence of localizable disease.*	Nonstimulated Tg > 5 ng/ml or Stimulated Tg > 10 ng/mL or Increasing Tg values over time with similar TSH levels or Rising TgAb levels And Negative imaging
Structural incomplete response: *Persistent or newly identified loco- regional or distant metastases with or without abnormal Tg or TgAb.*	Structural or functional evidence of disease regardless of Tg or TgAb
Indeterminate response: *Non- specific biochemical or structural findings which cannot be confidently classified as either benign or malignant.*	Non- specific findings on imaging studies or Faint uptake in thyroid bed on RAI scanning or Non-stimulated Tg 0.2 - 5 ng/mL or Stimulated Tg 2- 10 ng/mL, or TgAb levels stable or declining in the absence of structural or functional disease

<0.2 ng/ml

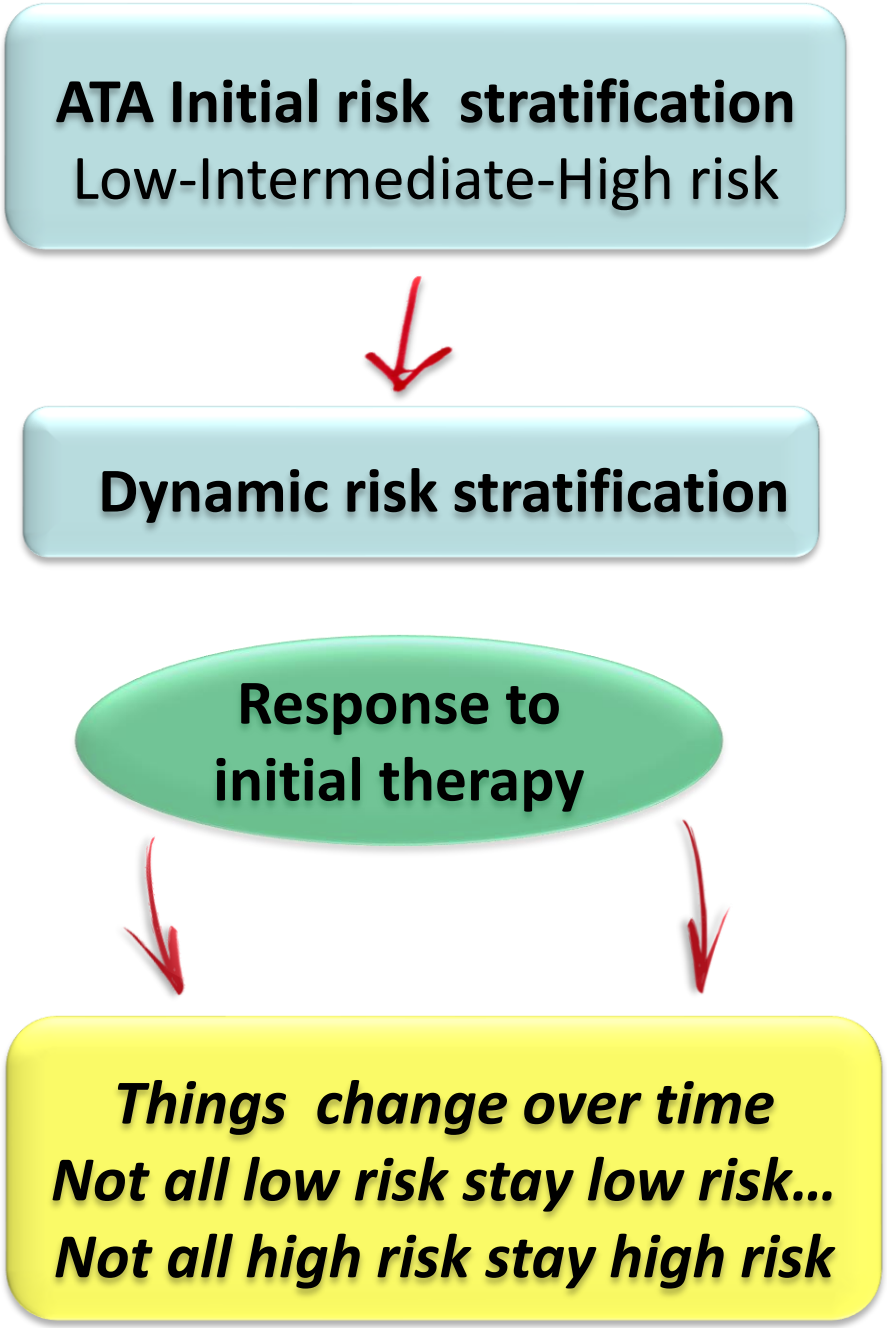
>5 ng/ml

0.2-5 ng/ml

Response-to-therapy Reclassification in Differentiated Thyroid Cancer Patients Treated with

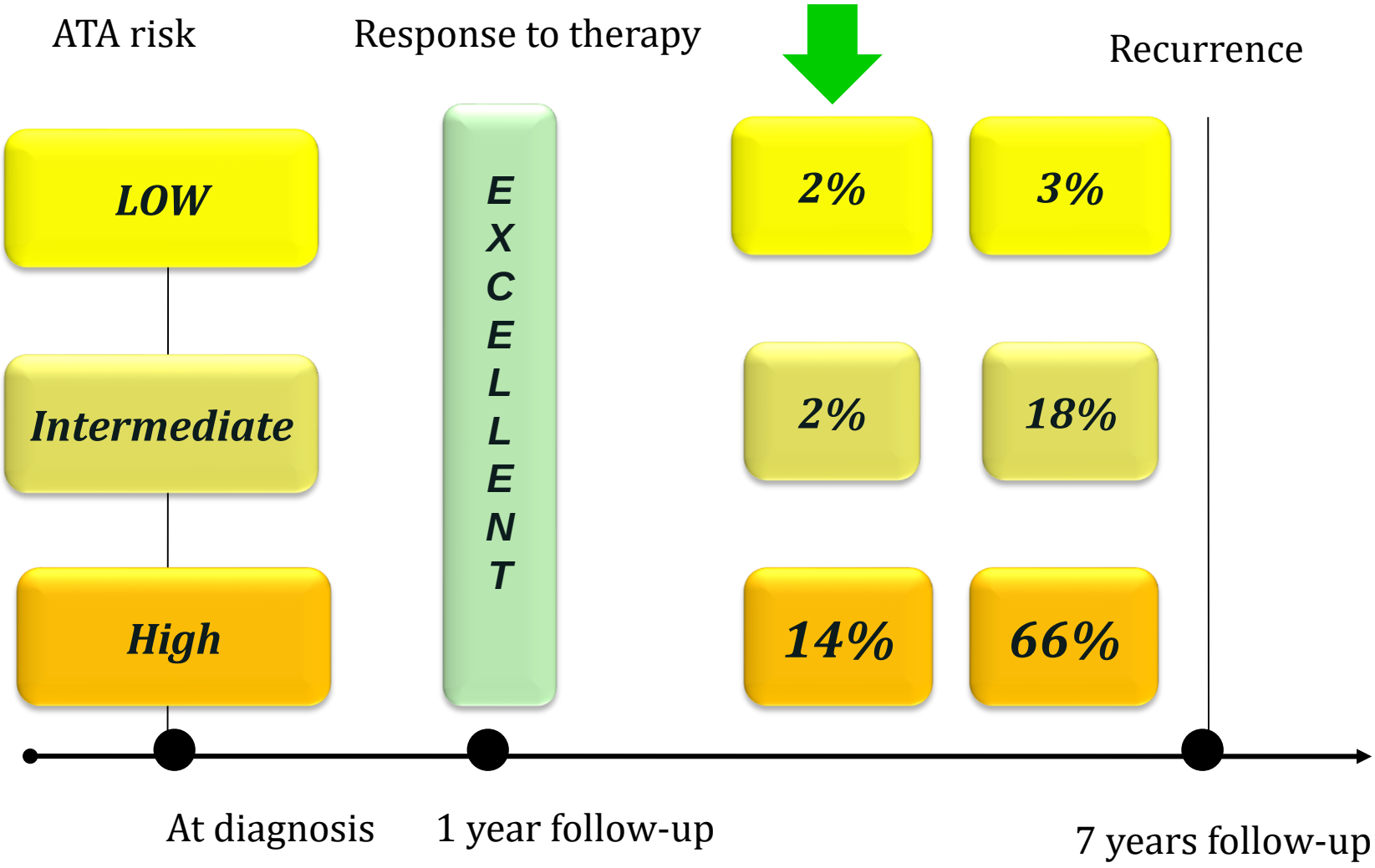
Total Thyroidectomy without RAI Remnant

Momesso, JCEM 2016



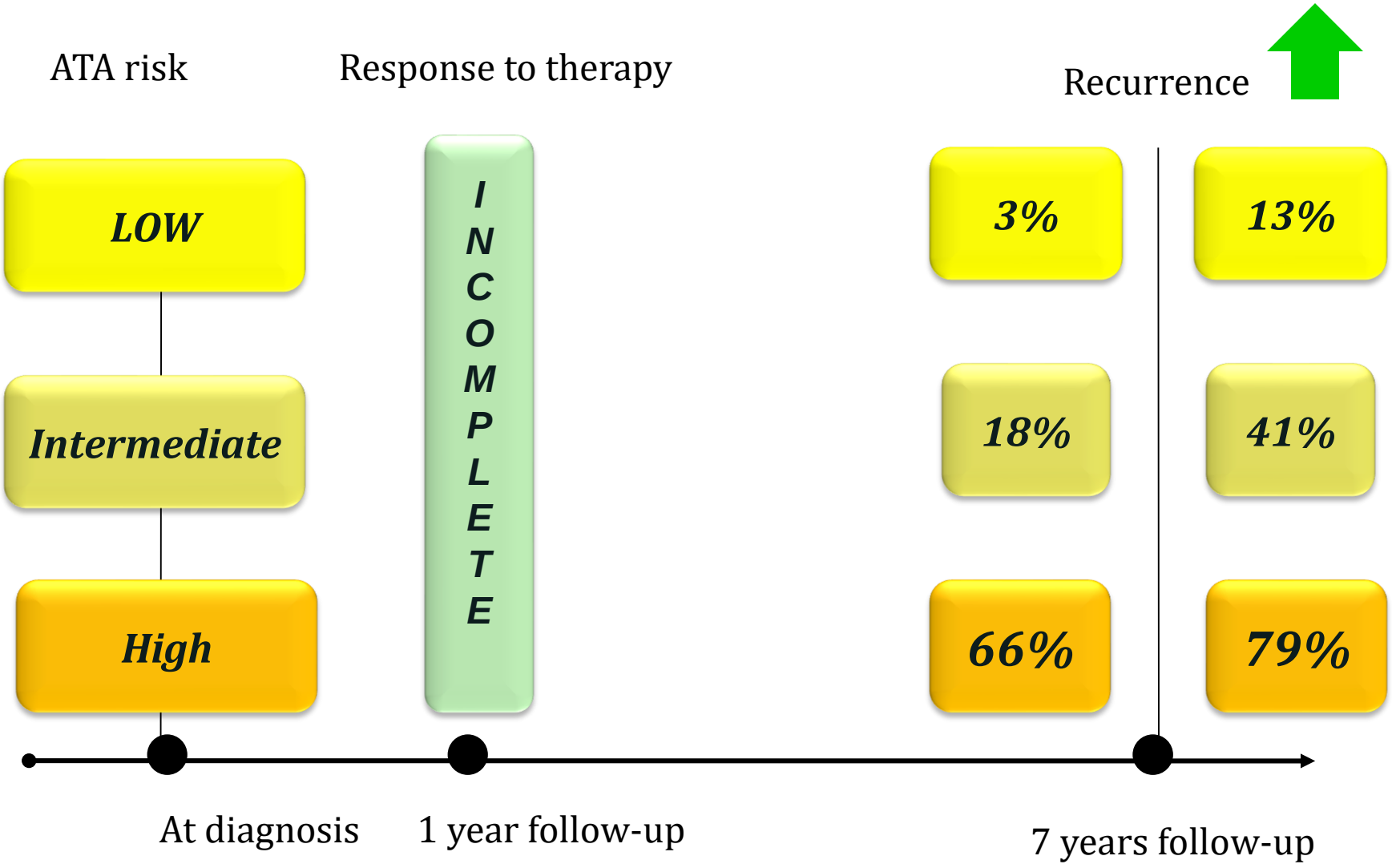
2015 ATA Guidelines, Haugen et al, Thyroid 2016

Risk of recurrence



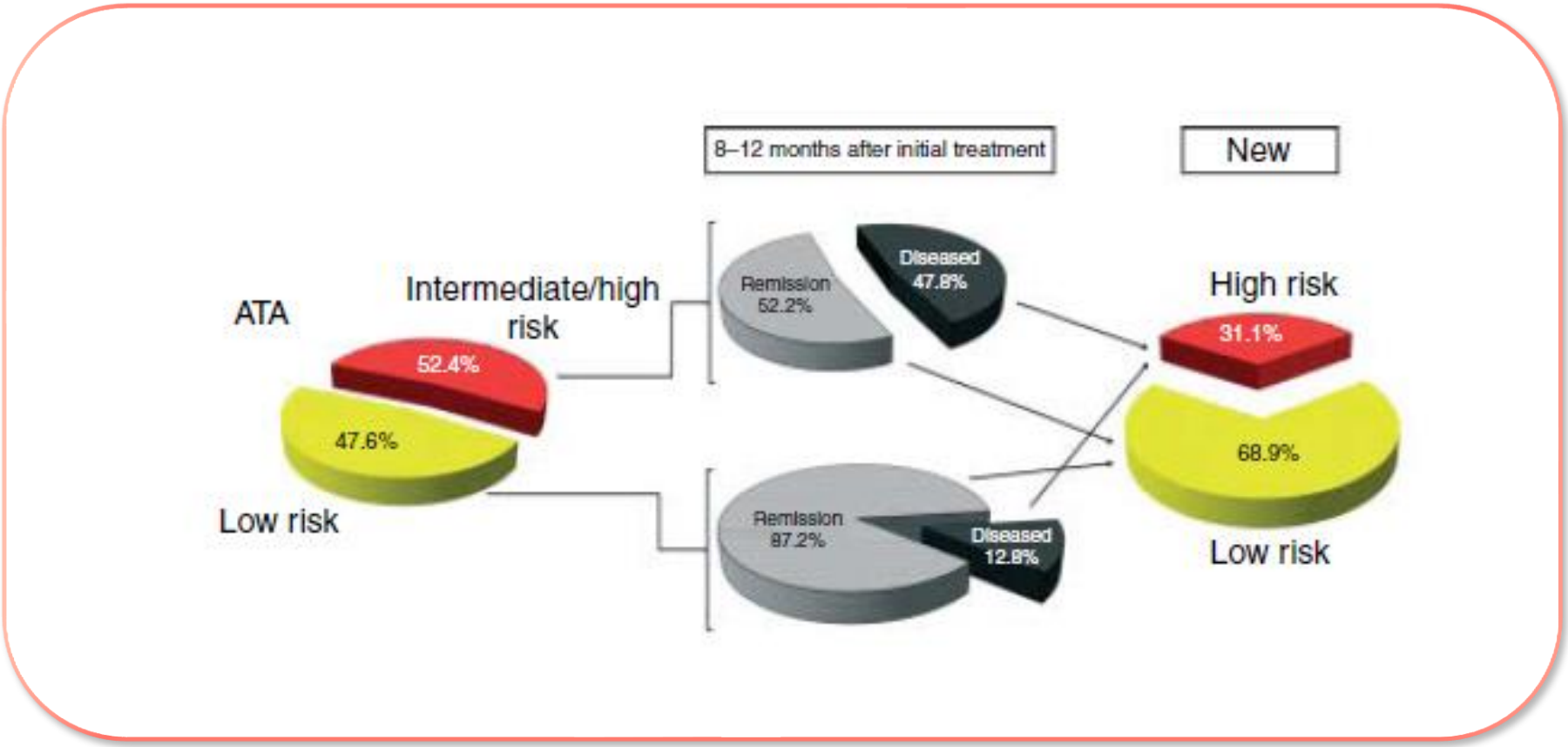
Tuttle, Thyroid 2010

Risk of recurrence



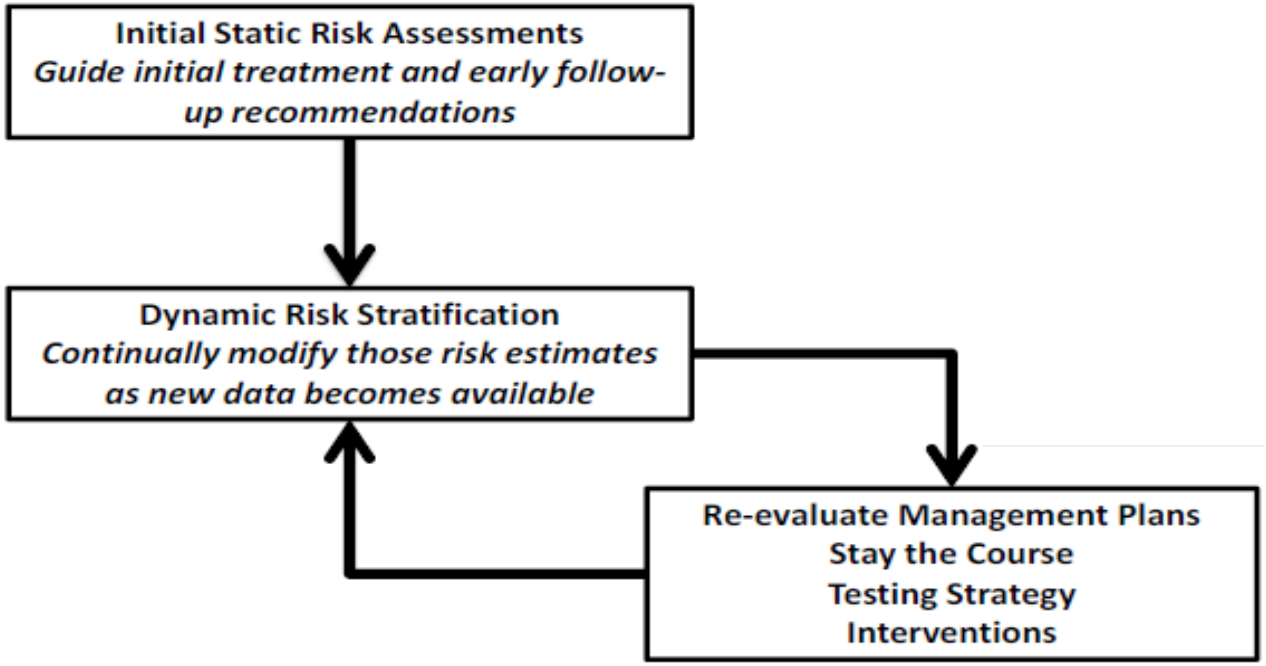
Tuttle, Thyroid 2010

Delayed risk stratification, to include the response to initial treatment (surgery and radioiodine ablation), has better outcome predictivity in differentiated thyroid cancer patients



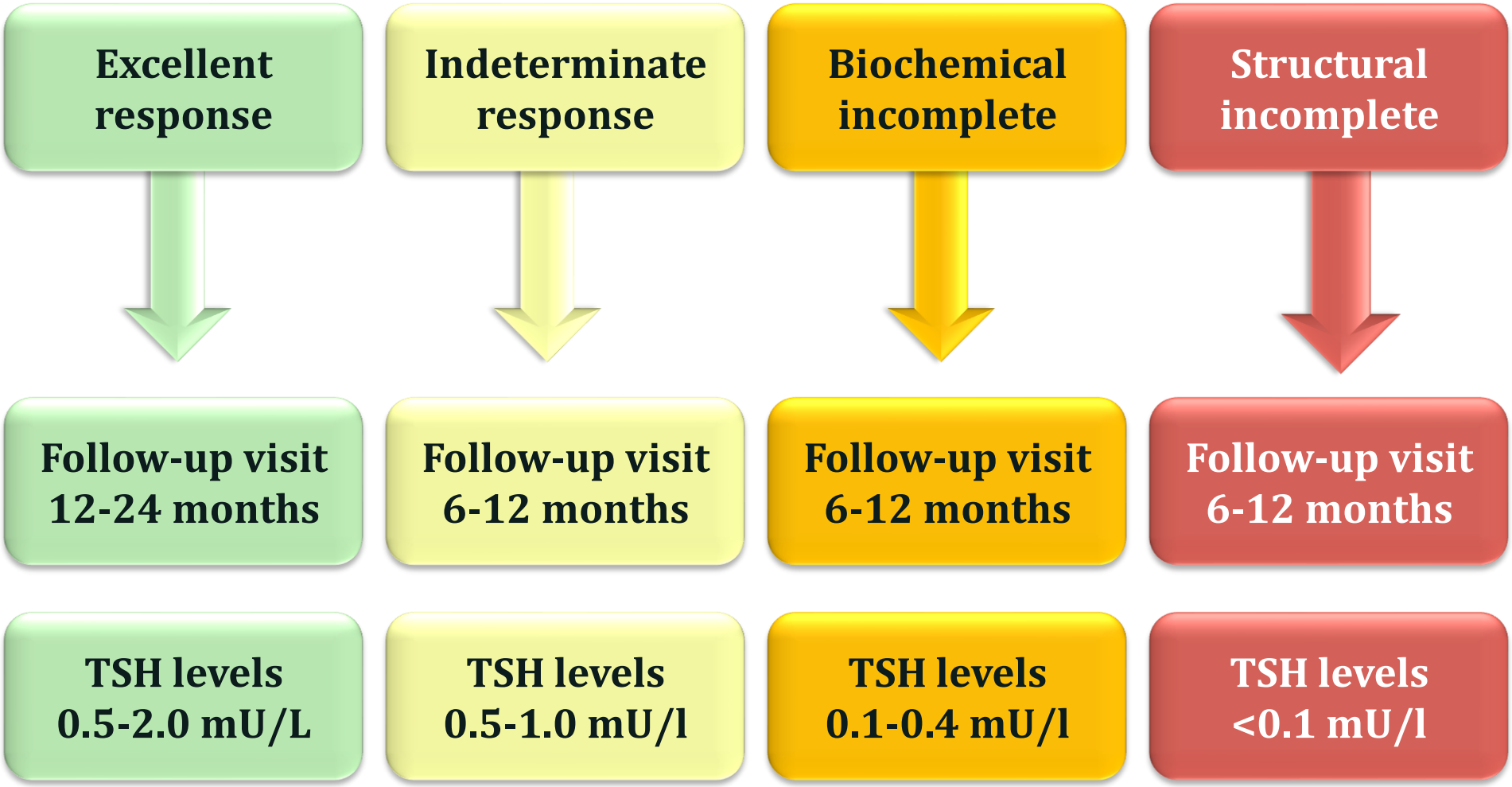
Castagna et al, EJE 2011

Il follow –up con la stratificazione dinamica del rischio



This approach allows the individual patient's clinical picture to change from a fuzzy image at initial diagnosis to a sharp crisp picture as new data are obtained over time

Clinical implication of response-to-therapy reclassification in DTC treated with total thyroidectomny and RAI remnant ablation



ATA guidelines 2015


Grazie per l’attenzione!
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